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JOURNAL INTERVIEW 29

Conversation with Sir Richard Doll

In this occasional series we record the views and personal experience of people who have specially contributed to the evolution of ideas in the Journal's field of interest. Sir Richard Doll and his colleague, Sir Austin Bradford Hill, established in 1949 the relationship between smoking and lung cancer, their findings being published in 1950 in the British Medical Journal.

BJA: *I want to establish the antecedents for your later research contributions. You qualifed in medicine in 1937 at the age of 24?*

RD: Yes, I qualified through the Conjoint examination early in 1937 then took the London MB BS exam in June. I had gone straight from Westminster School to St Thomas's Hospital, but I had decided to do medicine only very late. The thing that gave me real pleasure at school was mathematics. I took A levels, Higher Certificate as it was in those days, in mathematics. I wanted to go to Cambridge to read mathematics, because I was told it was the best place for the subject and I tried to get an open scholarship. I sat the scholarship exam and did well on the first papers, but very badly on the last one. The tutor for admissions rang my father and said they couldn't give me the scholarship because of my last paper, but would I take an exhibition. I was so annoyed with myself—the reason I did so badly on the last paper was, in fact, because I had drunk too much of the strong Trinity College ale the night before—that I told my father that I wouldn't go to Cambridge to read mathematics but would do what he had always wanted me to do, which was to study medicine. It was essentially an emotional reaction, but I have often thought that the ale which I drank on my last night in Cambridge was the best drink I ever had! I then had to study biology quickly. But I really didn't mind what I did as long as it was something scientific. I had always respected my father's work as a GP and was, in consequence, happy to do medicine. I got into St Thomas's the next year and have enjoyed every minute ever since.

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BJA: At St Thomas's was there in those days any opportunity for a medical student to engage in research?

RD: No, there wasn't. But we had, as most medical schools had, a journal that was produced periodically—the St Thomas's Medical School Gazette —and I wrote an article on statistics in medicine, whilst a student, which recommended the use of Chi Square tests in medicine,[1] which was certainly the first time that this had been recommended at St Thomas's. What stimulated me to write this piece was that one of the surgeons was treating undescended testes with pituitary extracts as he had read a paper which reported that this treatment increased the proportion of children in whom descent of the testes would occur. The claim was that the treatment produced descent in about 70% of cases against the previous rate of about 63%, but numbers of cases were small. I was sceptical of the conclusion as I had maintained my intererest in mathematics and been reading Fisher's book on *Statistical Methods for Research Workers* which taught how to do a Chi Squared test, and application of the test showed that similar or more extreme differences could have turned up by chance about 6 times in 10. That was in 1936 I think. But we had no opportunities for doing research. My clinical interest then was neurology and I got very interested in electroencephalograms. I went and saw them being recorded by Grey Walter at the Maida Vale Hospital, and wrote an article on their use in medicine in 1937.[2]

BJA: *Is it apocryphal, I seem to remember Dennis Hill telling me, that as a medical student you pointed out that when it came to a measure such as haemoglobin,*

the mean wasn't enough and one had to think also of a standard deviation?
RD: It is quite likely although I don't actually recall it.

BJA: *When you qualified in 1937 did you think, "Now for a research career", or were you considering neurology? Obviously the war was imminent.*
RD: I had always wanted to do research but in those days you really couldn't do research unless you had a private income. The grants were very few, and very small when you did get them. What you had to do was to become a Consultant Physician, get on the staff of one of the teaching hospitals, and then you could make enough money and have the facilities to do some research. That was really what I was hoping to do.

BJA: *How did you spend those two years before the war started?*
RD: I got my London degree in July 1937 and then applied for a House Job at St Thomas's. I was fortunate enough to get one for a year: 6 months as Casualty Officer and Anaesthetist and 6 months as House Physician—so that took me through to 1938. I then tried to get a job at the Royal Postgraduate Medical School at Hammersmith, which was just beginning to get recognized as an outstanding centre for research. I went to see Fraser, the Professor of Medicine. His House job had been advertised but he said he couldn't offer it to me because he had promised it to someone else. However, if I were to do 6 months voluntary research at Hammersmith, I could be his House Physician when it next became vacant. This attracted me greatly, not least because it would pay me £100 a year. (At St Thomas' one had only free beer and free laundry.) In the meantime, however, I had to look for some way to earn a living, whilst I did the 'voluntary' research. Fortunately, a friend of mine suggested that I might share with him the job of Resident Medical Officer at the London Clinic. The reason they wanted a resident doctor at the clinic was that it advertised that there was always a doctor on the premises; but the last thing that any of the Consultants wanted you to do whilst you were there was actually to see any of their patients. They had, however, to have someone available the whole time. What was usually arranged was to have two resident doctors, one of whom was on call at night, and one who was on call during the day. This suited me very well. My friend was on call all day, while I worked at the Hammersmith, and then I was on call all night. This seldom interfered with my sleep (I was called only about 3 times the whole 6 months I was there) and it enabled me to earn sufficient money to keep myself while doing research at Hammersmith, under the cardiologist Paul Wood. My project was to develop a technique for measuring vitamin B1 in the urine as Wood had the idea that rather more heart failure might be due to alcoholism than was generally recognized and that B1 deficiency might be an indication of excessive alcohol consumption. The technique proved too difficult for me. I had to grow a fungus on blood, the amount grown being dependent on the amount of B1 in the substrate, but I could never get reproducible results and nothing came of the work. The only other interesting thing that I did at the time was to look for a factor in blood responsible for hypertension. In those days hypertension was thought to be a unitary disease. I took blood from a patient who was having a nephrectomy because of hypertension due to renal disease and gave it to another patient to see if his blood pressure would go up, but the blood clotted and the experiment was not a success.

BJA: *So then the war came?*
RD: It came very soon after I started the House job. I started with Fraser at the beginning of August (or rather with Stuart Harris who was acting for Fraser during his holiday) and was called up on 1 September. This was because I had joined the Supplementary Reserve after Munich, when it became obvious that there was going to be a war.

BJA: *You were in the army all the way through from 1939 to 1945?*
RD: Not quite to the end of the war. I got renal tuberculosis in the middle of 1944 and was discharged early in 1945 after a nephrectomy. The tuberculosis fortunately turned out to be unilateral.

BJA: *I've read your recent BMJ articles. Tell us about your adventures around the time of Dunkirk. What happened to you after that? Did you remain on Regimental duties or were you in any research position?*
RD: I stayed with the Battalion for a few months and then, presumably because I had obtained the MRCP in the summer of 1939, I was posted to a hospital in Shaftesbury, where I worked for 3 months before being posted to the Middle East, as a member of a group of medical reinforcements. Before leaving I had a fortnight's course in tropical medicine in Liverpool, during which time it was blitzed fairly

heavily, and I left for the Middle East in January 1941. I first worked there as a Captin in charge of the medical side of a small hospital in Cyprus. I was there for a year and after the fall of Crete it was quite an interesting place to be. At the time, there was no animosity between Greeks and Turks. The Greeks, who wanted union with the mainland, were content to discuss it in a civilized way over a cup of coffee or a glass of ouzo. Then I went back to Egypt, to the 63rd General Hospital at Helmieh, where I was eventually promoted to medical specialist and took charge of the ward for serious infectious diseases—diptheria, typhoid, typhus, poliomyelitis, and small-pox being the most important. I was there for 18 months before being posted to a hospital ship which spent its time sailing up and down the Mediterranean. We took part in the invasion of Sicily and the invasion of Italy, taking troops off the beachhead at Salerno, but much of the time we were sailing empty or transferring sick men from one port to another. Altogether it was one of the most enjoyable years of my life.

BJA: *You weren't being bombed or shot at?*
RD: The Germans were scrupulous in respecting the Red Cross on hospital ships in the Mediterranean. The ship I was on had been refitted in Alexandria after being hit by a torpedo from a submarine before I was attached to it. When the British protested Rommel asked if we could reasonably expect anything else when our hospital ships sailed without lights immediately behind a convoy. He assured us that if we sailed with our lights on and broadcasted our position we would be alright. So all that year we did. Many German planes came down and had a look at us and went away. The only time we were in any danger was when we were in harbour or backing up the landings when obviously we were part of a fair target. But Rommel was quite scrupulous in his adherence to international rules on the open sea.

BJA: *So you came out in 1945 because of your kidney. By that time you were 32. Were you still thinking of a consultant job with a bit of research? Or had the war influenced your career choice at all?*
RD: I wasn't discharged from the army until early 1945, but I had already worked for 6 months during convalescence. I had been advised to take things easily so I convalesced at Roffey Park, a rehabilitation centre, but as a doctor, not as a patient. There I decided that psychiatry was certainly not the subject for me. It was too difficult. I felt that one was putting oneself in the position of God and I wasn't very good at it. I then got a job at St Thomas's as a Junior Medical Assistant to the Professorial Unit. I worked there for the whole of 1945. I didn't get on very well with the young people who held senior positions to me in the hospital. They assumed that, having spent 5 years in the army, I knew nothing about medicine. Indeed, it was true that I wasn't as up-to-date as they were, but I did have rather more clinical experience. Later many doctors began to be released from the army and I found the atmosphere rather unpleasant. Everyone was trying to become friendly with the senior staff in the hope of being given one of the very few hospital appointments that were available at that time.

BJA: *Did you succeed in doing any research at St Thomas's?*
RD: Yes, a bit. Professor McSwiney, the Professor of Physiology, tried to get me interested in respiratory physiology and its application to clinical medicine, but the subject didn't attract me. I did, however, complete one piece of research to test the idea that one could relieve severe asthma by administering a mixture of helium and oxygen. The hypothesis was that the helium molecules, having less mass than nitrogen and oxygen molecules, would make a mixture of oxygen and helium easier to get into the lungs than either pure oxygen or oxygen and air. It ignored, however, the complexities of streamline and turbulent flow and the independent diffusion of different gases, but it was claimed to be supported by empirical observations. However, when I sat by the side of patients switching from one mixture to another, some actually got worse on the helium mixture.[3] I also tried to do some research on the effects of labour on women with heart disease, although I never wrote this up. At that time advice was being given as to whether or not a woman should become pregnant if she had heart disease, in what I thought was a very unscientific way. The obstetricians were also very unhappy about it. So I used to follow all pregnant women who had any form of heart disease (mostly rheumatic in those days), and again make detailed observations on how they got through their labour, with a view to being able to give better clinical advice as to whether or not a woman could have a baby.

BJA: *So you were clearly making a start on a research career but you say that you were unhappy with the competitive atmosphere prevailing at St Thomas's. How did you find a way out?*

RD. A young friend of mine, to whom I was subsequently married, was Dr Joan Faulkner. She was working at the Medical Research Council's headquarters and when I told her of my desire to find a research job she said that the MRC were wanting to support some research by Dr Avery Jones at the Central Middlesex Hospital, but that they couldn't find a suitable person to work with him. I went to see Avery and we immediately got on well. I started to work with him on a grant which he was given to study occupational factors in the aetiology of gastric and duodenal ulcers. From then on everything went very easily. We designed a survey of the prevalence of peptic ulcers in men employed in different industries in the neighbourhood of the Central Middlesex, with which Avery had already developed contact. We appointed a social worker as an assistant, who interviewed all the workers and obtained an indication of whether they had ever suffered from indigestion by the use of a standard questionnaire. I then saw all the workers with any suggestive evidence of indigestion plus a 10% sample of those with none to ensure that the screening procedure was satisfactory. We managed to interview 98.4% of a total of some 5000 workers. The work was reported to a committee under the supervision of Professor Ryle, with Bradford Hill as one of its members. Bradford Hill was very impressed with our having obtained a 98.4% response rate, because a number of studies in occupational medicine in those days had been content with a 60 or 70% response and, after I had taken the course in medical statistics at the School of Hygiene, during the time I was working on Avery's project, Bradford Hill asked me if I would like to work with him on a study to try to find out the causes for the increase in lung cancer. This was to begin in January 1948, when Avery Jones' grant expired.

BJA: *What is your sense of the climate of medical ideas on the relationship between smoking and lung cancer at that time?*

RD: The starting point of our study was the increase in the number of deaths that were attributed to lung cancer. It was Percy Stocks, the Chief Medical Statistician at the Registrar General's office, who drew the MRC's attention to the dramatic increase in the number of these deaths. As a result the MRC held a conference in 1947 to consider whether the increase was real and if so whether anything could be done to find its cause. Following this, a small committee, consisting of Kennaway, Stocks and Bradford Hill, was set up to design a study to look into the reasons for this increase. While it could not be proved that this increase was real, there was much to suggest that at least part of it was, and in any case, it would have been very unwise to assume the increase was wholly artificial, in case some real increase had actually occurred. Plans were, therefore, drawn up by Bradford Hill, Kennaway, and Stocks for a study to be carried out by Bradford Hill with a research assistant, which I was fortunate enough to become. What we did was to list all the possibly relevant factors that we thought people could have been exposed to and which could have become more prevalent over the previous 50 years. There weren't very many and one of them was smoking and particularly the smoking of cigarettes. Kennaway was particularly interested in the possibility of smoking being a factor, but I don't think anybody else was. Bradford Hill certainly wasn't particularly keen on smoking as a cause, nor was I, while Stocks was particularly keen on the effect of general urban atmospheric pollution. I must admit that I thought that the latter was likely to be the principal cause, though not pollution from coal smoke which was terrible in those days but which had been prevalent for many decades and hadn't really increased. In fact coal consumption had already begun to diminish. Motor cars, however, were a new factor and if I had had to put money on anything at the time, I should have put it on motor exhausts or possibly on the tarring of roads. Because of course the whole road system in the country had changed with the advent of the motor car and we knew from Kennaway's work that the tar that was put on the roads contained many carcinogens. Various industrial developments were another possibility. We also thought of arsenic, which had been increasingly used in the treatment of syphilis, as a possible factor, although we weren't able to test this idea very effectively. But cigarette smoking was such a normal thing and had been for such a long time that it was difficult to think that it could be associated with any disease. Indeed in the medical textbooks of the time the only effects of smoking that were described were tobacco amblyopia—which is a disease that opthalmologists now tell me doesn't occur, but which could have been produced by heavy pipe smoking in the presence of dietary deficiency—and tobacco angina: that is, angina precipitated by smoking which was so rare that individual cases were written up.

BJA: *Was there no interest in the possibility of pipe smoking and cancer of the lip?*

RD: Yes, that association and the association with cancer of the tongue were really pretty firm. They were, however, more often thought to be due to the heat from the pipe stem than to the tobacco. Indeed, I remember asking our senior surgeon when I was a student, when we saw a case of cancer of the tongue in out-patients, whether he thought pipe smoking or syphilis was the cause (cancer of the tongue being commonly observed in association with syphilitic leukoplakia). Mr Maybury replied that he didn't know whether either was the cause of the disease, but he did know that the wise man avoided the combination of the two. These risks were fairly generally accepted, but not to the extent that people were advised not to smoke pipes.

BJA: *You then took your research forward and interviewed quite a large sample.*

RD: We actually ended up interviewing 3500 patients, including some 500 in rural hospitals because we wanted to get estimates of smoking habits in different parts of the country. But the main study was based on some 2900 patients in London and four other large cities.

BJA: *The technique was to go along with a questionnaire to hospitalized patients who had not got lung cancer and ask them about possible antecedents and compare their answers with those from patients who had got lung cancer?*

RD: That's right. Sir Harold Himsworth, the Secretary of the Medical Research Council, or rather Dr Green, his number two, wrote to 20 London hospitlas and asked if they would collaborate by allowing us to see patients in their wards. We set out to see patients not only with cancer of the lung, but also others with cancer of the stomach or large bowel and a control series of patients with other diseases. One reason that we included patients with two other types of cancer was because it was hoped that the interviewer would not know which type of cancer the patient had, so that we could avoid bias due to knowledge of the nature of the patient's disease. The second reason was that we wanted to see if any factor that was associated with cancer of the lung was associated with cancer generally, or was specific to cancer of the lung. We employed four medical social workers, or Almoners as they were then called, to interview the patients, as only Almoners were acceptable to the medical profession. Nurses in those days didn't interview patients. The four Almoners visited the hospitals weekly and went to the wards asking if any patients with these diseases had been admitted. We also had a system by which hospitals notified us of the admission of the sort of patient in whom we were interested. But by and large we found that the best thing was just to visit frequently the wards where we knew the relevant patients might be.

BJA: *Your role was the organization of this study. You weren't having to do the interviewing.*

RD: No, I didn't do any of the interviewing. It was of course my job with Professor Bradford Hill to design the questionnaire, to check the results of the interviews as they came in, and to see that we were getting the right number of controls matched appropriately with these cases. Then of course I had to check the diagnoses. We interviewed patients who were admitted with a diagnosis of "query lung cancer, stomach cancer or large bowel cancer". So every diagnosis had to be checked after the patient left hospital. This was important, not only to check the diagnosis but also to obtain information about the histology and the part of the lung in which the tumour originated. We soon found that many of the patients interviewed in the belief that they had lung cancer turned out not to have it. These constituted an excellent second control group, for they would be subject to the same bias, if any existed, as affected the results of the interviews with the patients who actually had lung cancer. As I went through and checked the diagnoses I saw that patient after patient in the 'lung cancer' group who was regarded as a non-smoker turned out not to have lung cancer; whereas, in those who were heavy smokers the diagnoses seldom had to be changed. The non-smokers in the lung cancer group just melted away when we came to check the diagnoses—they might have anything from fibrosarcoma of the chest wall to bronchiectasis, but they didn't have lung cancer. This was a striking finding and quickly drew our attention to the importance of smoking.

BJA: *What was the statistical technology, how were you handling this really very considerable mass of data in the days still of hand-driven calculators'*

RD: I didn't even use a calculating machine: I just listed the results in a book. Our questionnaire was relatively short as it was always part of Bradford Hill's teaching to keep questionnaires brief, and I've always tried to ensure that interviews should take less than half an hour. I have unfortunately failed in recent years, but for that first study we succeeded. I then extracted personally, from each form, the information that looked as if it might be of interest,

entered it in columns in a record book, and added up the numbers in the columns. The whole thing was done with a 19th century clerical technique.

BJA: *You were getting some idea as to the excitement of the work from finding that the false diagnoses related to the non-smokers. But the real excitement must have been when you added up those columns and figures and did the first Chi Square. Back to your beloved Chi Square?*

RD: Well no, we didn't really need to do a Chi Square, the answer was so clear (but we did, of course, do one for publication). We started interviewing in 1948 and by the beginning of 1949 Bradford Hill and I were quite convinced that there was a strong association between lung cancer and cigarette smoking and not much of an association with any of the other factors we were interested in. When we had data on some 650 male patients with lung cancer we wrote up the results. We came to the conclusion, for the reasons which we set out in the paper, that we had found an association that we believed indicated cause and effect.[4] We reached that conclusion in 1949; but we took that paper to show Sir Harold Himsworth before submitting it for publication, because we realized that the conclusion was dramatic and Bradford Hill and I both had the greatest respect for his opinion. Himsworth said that the finding was so important that he didn't think we should publish it until we had found it again in a second series. He pointed out that the study had been entirely limited to patients in London hospitals and he wondered if there could be something speical about London that produced the result. He wanted to see results from elsewhere in the country as well. So we didn't publish, but arranged instead to interview patients in Bristol, Cambridge, Leeds, and Newcastle. We continued the study and we expanded it to cover over 1400 lung cancer patients.[5] Whilst we were still collecting the second set of data and it had become obvious that the results in these other towns were going to be the same, Wynder and Graham published their paper in the *Journal of the American Medical Association*.[6] That of course had the same effect as our check on patients in other towns. We went to Hugh Clegg, the Editor of the *British Medical Journal*, with whom Bradford Hill was on very good terms, and asked him if he could publish our paper quickly. He said that he would get it out in a matter of weeks and he did.[4]

BJA: *Did you know the Americans were on your tail?*
RD: No.

BJA: *It must have been rather a nasty moment, wasn't it?*
RD: It was disappointing, yes. We'd had this result for at least 9 months and had been sitting on it. But I don't regret having done so, because I think that the principle was right. It was a principle that I have tried to adhere to ever since: namely, that if you find something that is unexpected and which is going to be of social significance you have a responsibility to be sure that you're right before you publicize your results to the world. This does at least require repeating some of the observations.

BJA: *Firstly with Avery Jones and then with Bradford Hill you had come into contact with outstandingly able scientists. Had you been looking for a distinguished senior person to work with or was this just good fortune?*
RD: It was just good fortune. I knew as a young man wanting to make a career in research that one would have to work with someone who could set you on the right lines. I was happy to have gone to Avery Jones to work in the field of gastroenterology. He was a marvellous person to work with and I continued working with hime for 20 years after I joined Bradford Hill. During all this time I continued with clinical research for 2 days a week at the Central Middlesex Hospital. So I wasn't actively looking for someone else to work with. I had quite anticipated that I could go on doing research with Avery Jones. But this offer from Bradford Hill was very exciting. Bradford Hill was by then established as a leading figure in medical science in this country from whom one could learn a great deal, while Avery Jones still had to make his name. The opportunity of working more in the statistical field and of being able to paly with numbers a bit more was also very attractive, so I was just delighted by the opportunity.

BJA: *So that crucial paper came out in the BMJ in August or September 1950?*
RD: I think it was September.

BJA: *As you clearly foresaw, it was going to have a considerable social impact in the early days of the National Health Service. I will come back later to the continuation of the research. Let's just deal with the social impact for the minute. That work was published in 1950 and I think it was 1957 before any Minister of Health stood up and took it seriously. Were you disappointed, furious, or did you feel that it was not a research workers job to do other than*

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RD: I was fortunate again in being associated with Bradford Hill at this time because I think he had the right attitude, and I have subsequently tried to model mine on his. His attitude was that the research workers's job is to obtain the results, to report them, and to comment on them if he is asked to, but to leave it to other people to act on them. The reason Bradford Hill gave for having this view was that if you once started aying what ought to be done with your own results you might get emotionally attached to them, whereas, as a research worker, you always ought to try to disprove your own findings. That indeed was what we set out to do. Having said then that in our view cigarette smoking was a cause of carcinoma of the lung, we tried to think how the conclusion could be disproved. Bradford Hill had the idea of asking doctors what their smoking habits were, then following them up and seeing whether we could predict which of them had the greater risk of developing cancer of the lung. If our original findings had been wrong we should not be able to do so. We therefore started our second major project which was a cohort study of some 40 000 doctors from whom we had obtained details of their smoking habits. The American Cancer Society's similar cohort study was started by Hammond shortly afterwards with the specific intention of disproving the conclusion of our case-control study, which he told me he did not believe. He started the American Cancer Society's study[7,8] to show that we were wrong. We started our cohort study, not to show that we were wrong, but to see if we were wrong.[9–11]

BJA: *So in 1951 the first cohort was inteviewed?*

RD: Yes. We decided to do this in the summer or spring of 1951. We wrote first of all to a random sample of doctors. It wasn't, in fact, truly random: we just took the first name at the top of each left-hand page of the medical directory until we got 200 names. It so happened that Sir Harold Himsworth's name was one of them. When we sent him the questionnaire he refused to believe that he was part of a random sample! The idea of the pilot study was to see whether doctors would respond. As they responded well, we decided to launch a major study. The British Medical Association agreed to help us. They provided the addresses of all the doctors in this country and sent out the letter and questionnaire that we had prepared.

BJA: *The reasons for choosing doctors?*

RD: We chose doctors for very good reasons. First, we hoped they would be more interested than the general public and would respond more readily. Secondly, we hoped that having had some scientific training they would be more accurate in their replies. But thirdly, and most importantly, we thought that they would be easier to follow-up. Doctors kept their names permanently on the Medical Register so that you could know where they were and could keep tabs on them more easily than on a sample of the general population. As a result we found that even after 20 years we could trace 99%. So for all those reasons the choice was a good one. In fact, it turned out to be an even better choice than we realized because doctors were, I suspect, convinced by the results obtained from their own colleagues more easily than they would have been if the subjects of the study had been any other group. At any rate the British medical profession accepted the results and acted on them long before the medical profession did in any other country.

BJA: *You mailed them in 1951 and then carried out a number of waves of follow-up?*

RD: Yes. We mailed them at the end of October and regarded the study as starting on 1 November. We have, in fact, sent them further questionnaires about six times. Our published results are based on records obtained in 1951, 1957, 1962 or 1963, and 1971, but we also wrote to them again primarily for another purpose in 1978 and 1979, and to a sample just in the last year. Getting new information has proved to be very important because there has been such a big change in habits.

BJA: *Can you recapitulate in essence what you think the findings have been from the doctors study?*

RD: Before answering that I should like to make just one comment on our case-control study, which is I think of some interest. It illustrates how very little attention was paid to smoking as a possible cause of disease in the late 1940s. When we chose our control patients, we obviously wanted to exclude patients whose disease might be due to smoking. Yet, the only patients we excluded were patients with cancers of the lip and tongue, which you referred to earlier; and patients with cancers of the mouth, pharynx, oesophagus, and larynx, as there was a little evidence relating pipe smoking to cancers of parts of the upper respiratory and digestive tracts. So we excluded those patients but we included

patients with coronary thrombosis and even patients with chronic bronchitis. There was no suggestion among chest physicians in the late 1940s that chronic bronchitis could be due to smoking, although they of course recognized the existence of 'smokers' cough'. Today that's almost impossible to believe. We fortunately didn't have such a high proportion of patients with these diseases in the control group as to invalidate the study. But when we broke down our controls into groups with different categories of disease, we did find that those with respiratory disease smoked a little more than the rest of the population. We didn't, however, have any inkling that coronary thrombosis might be linked to smoking until we had the early results of the cohort study of doctors, the very first results of which indicated that such an association might exist.[9]

BJA: *That's very interesting. Going back then to the nub of the findings of the cohort study...*

RD: We published some results very early on, I think it was after 29 months of follow-up.[9] This was as soon as we got a statistically significant excess of lung cancer in cigarette smokers. We thought we should publish that straightaway to show that the case-control results were confirmed. Then we had more solid results in 1956, by which time we had some 50 months of observation. By this time too we had also found an association with chronic bronchitis and the association with coronary thrombosis was clear.[10] Of course by then the American Cancer Society had also shown the relationship with coronary thrombosis which they had concluded was causal.[7] The other outstanding finding in the cohort study was that the quantitative relationship with smoking was almost exactly the same as we had found in the case-control study. This showed that you could get not only qualitative but also quantiative estimates of risk from a case-control study. As we got more data, so the dose–response relationship became firmly established and we found it to be practically identical with that deduced from the case-control study.

BJA: *But what you could get out of your cohort study which you could never get out of a case control was the impact of stopping smoking?*

RD: That's not entirely true. The case-control study has shown that ex-smokers were less at risk and were relatively less at risk the longer they had stopped. But what one couldn't get out of that study was the precise temporal relationship between the change in risk and the abandonment of the habit. Indeed now, after all these years, I still find that there are scientists who do not appreciate what the temporal relationship actually is. This is because many publications have shown only the relative risk in comparison with that in non-smokers and how this changes with the passage of time. If you present a graph showing the relative risk in current smokers and the trend in the relative risk in ex-smokers with the passage of time after stopping, all compared with the risk in non-smokers, you see a progressive reduction in ex-smokers with the relative risk gradually approaching unity. But this doesn't mean that the risk actually falls. What you are showing is a fall relative to that in non-smokers. Lung cancer, however, becomes more common in non-smokers as people age and if you plot the risk, not as relative to that in non-smokers but as an absolute risk, what you find is that the risk when you stop smoking first ceases to increase, staying more or less constant, and then slowly increases; because, after all, the ex-smoker is exposed to the same factors that cause lung cancer in non-smokers. What happens is that the curve approaches the curve for non-smokers asymptotically, which means that the risk increases in much the same way as the risk to non-smokers. So it is quite untrue to say that the risk falls when you stop. It is conceivable that there is a small drop for a few years after smoking is stopped, but the data are not enough to be sure whether there is a small drop or whether the risk remains more or less constant until the factors that cause lung cancer in non-smokers begin to cause an increase in the ex-smokers. That is not to say, that it is not worth stopping. It is immensely worth stopping at any age. For if you continue the absolute risk increases dramatically with the passage of time and the ex-smoker is at much less risk than if he had continued, within only a few years.

BJA: *Your major research thus employed just two functionally linked strategies?*

RD: In a sense, yes. But there is a point that is sometimes overlooked; our results were interpreted in the light of all the other available epidemiological information. We would never have said, on the case-control study alone, that cigarette smoking was a cause of carcinoma of the lung. We were as aware as many of our critics have been that an association doesn't necessarily imply causation and that the association we observed might have been due to an association between smoking and exposure to some other agent or to some other type of behaviour that

was actually causing lung cancer, or even, as Fisher suggested, to an association between the tendency to smoke and a general susceptibility to the disease, although I must say that the last never seemed to me at all likely. We concluded that the association was causal only when we saw that it made sense in the light of all the other information that was available. For example, it made sense in the light of our knowledge of the sex ratio of the disease at different ages. It made sense of the fact that the disease was extremely rare in Iceland and very rare in Norway, when we found out that cigarette smoking had not been introduced into Iceland until the 1930s and that it had been uncommon in Norway. Then we found that the disease was particularly common in Finland and Austria, two countries which we knew had introduced cigarette smoking early on. We looked all around the world to see if we could find any evidence of a population who did not smoke but had a high incidence of lung cancer; there wasn't one. Similarly we looked to see if there was any area where smoking had been common for a long time and where there was a low incidence of lung cancer; again there wasn't one. I would prefer, therefore, to say that we also used a third ecological strategy. In sum, a causal relationship made biological sense in that there was a lower risk in lighter smokers than in heavy, a lower risk in ex-smokers, a lower risk in people who started to smoke later in life, a lower risk in women than in men, and a lower risk in communities in which cigarette smoking was rare. All this evidence enabled us to conclude that cigarette smoking was actually a cause of the disease. We said that in our first paper,[4] and the only credit I would claim for us is that we did pluck up our courage and state this openly. We believed that it was the sensible scientific conclusion.

BJA: *Let's go back to the question of the scientist as sticking to his lathe as scientist as opposed to the scientist entering as advocate in the public arena. When it came to the Royal College of Physicians's report in 1962, the Secretary was Charles Fletcher and the Chairman was Platt. Now you were not on that Committee. Did you refuse to join it?*
RD: No. I wasn't asked to join it.

BJA: *Wasn't that extraordinary?*
RD: No. It was, I think, done intentionally, because it was thought that the conclusion of the Committee would be stronger if it was independent of Hill and myself.

BJA: *But you must have been talking to Charles Fletcher and the others at the time.*
RD: Yes, but we didn't discuss that initial report. With subsequent reports I have been involved more, but that first report was prepared quite independently and I am very glad that it was. To go back a moment, if I may, about our conclusion on causality. We were entirely supported in this by Sir Harold Himsworth, whom I mentioned earlier and whose scientific ability I greatly admired. He refused to organize any further research on the question from long before 1957, which you mentioned as the time when the Ministry of Health first took the conclusion seriously. Himsworth had been repeatedly asked by the Department of Health to do more studies on the relationship between smoking and lung cancer, at the request of the Cancer Advisory Committee to the Ministry of Health, which didn't accept our conclusion. Himsworth, I think, as early as 1951[12] replied to the Department of Health and said that he wouldn't waste money on the subject as the matter had been proved. His backing from the day of our first publication was very valuable. Later, of course, in 1957, he got the Medical Research Council to state its support for our conclusion formally.[13]

BJA: *Did Horace Joules come and talk to you at the Central Middlesex?*
RD: Yes, of course. I talked to Horace frequently during my time at the Central Middlesex Hospital, where he was the Medical Director. He became, as you know, a powerful advocate of public education about the effects of smoking. He battled on the Central Medical Advisory Committee of the Department of Health from 1951 on. Every time the Committee had a meeting he asked it to make some statement about the effects of cigarette smoking but it always refused to do so. It wasn't until 1957, after the Government had formally asked the Medical Research Council for its opinion, that the Department accepted the conclusion.

BJA: *He was also a member of the Cancer and Radiotherapy Standing Committee.*
RD: Yes, and he certainly pressed it hard there.

BJA: *Are there any of the things you have mentioned which you would like to enlarge on?*
RD: There is the question of the attitude of the tobacco industry. This has been quite interesting. Soon after our publication the Chairman of the Imperial Tobacco Company, which was the leading

manufacturing company in this country at the time, asked to come and see us. He had brought with him a statistician by the name of Geoffrey Todd, and they challenged us over the correlation between lung cancer mortality and cigarette consumption in different countries. The correlation coefficient, they said, was only 0.5 and therefore we must be wrong. Bradford Hill replied that this sort of crude ecological correlation was very unreliable and that in his experience a correlation coefficient of 0.5 should be regarded as strengthening our conclusions. That rather set them back. They then said that smoking histories are too unreliable for us to have been able to draw any conclusion from them. That was easy, as any unreliability would merely weaken the real relationship. Finally, they said that the increase in mortality was more likely to have been due to the increase in atmospheric pollution. We didn't believe that there had been such an increase and, moreover, we had been unable to find much of a relationship with pollution in individual patients. When they left they initiated some research of their own. Five years later, Todd had found that people's smoking histories were recorded surprisingly accurately, and that habits were surprisingly constant and he was unable to make an association with atmospheric pollution stick. Todd then told the industry that we had convinced him that cigarettes were the principal cause of the disease. He told the Imperial Tobacco Company and the Research Council that the industry had set up, to which he was responsible, that unless they accepted the conclusion that smoking caused lung cancer, he couldn't work for them any longer. So they said thank you and goodbye. He took Joan and me out to dinner that day before he left telling us that it was the last expenses account dinner he would get out of the tobacco industry. Six weeks later he rang me and said that the industry had taken him back on his conditions. From that day on, for some years, we had a very good relationship with the tobacco industry in Britain. They agreed that they would not say anything to imply that smoking did not cause lung cancer or some other diseases, but they would continue to take the view that as people enjoyed smoking, they would continue to provide them with tobacco. So our relationship with the tobacco industry in Britain was initially good and all our contacts were both serious and polite. This, of course, ceased to be true when the power structure in the tobacco industry in this country changed and other influences came to determine its attitude. I wouldn't take the same view now.

BJA: *That's a very temperate statement to say that you wouldn't take the same view now. Would you take the opposite view?*

RD: I think that the tobacco industry in some other countries has behaved absolutely abominably. In this country BAT has behaved in a quite unacceptable way in some of the statements they have made. The situation now is quite different from what it was initially.

BJA: *What is your view on the current evidence on passive smoking. How convincing do you find the statistical evidence?*

RD: I have found this difficult to assess. Basically I agree with the conclusions of the working party on tobacco which I chaired for the International Agency for Research on Cancer.[14] Their conclusion was that environmental tobacco smoke contained many chemicals that were known to be carcinogenic to animals and that smoke was known to be carcinogenic to humans if breathed in actively, so that it must be assumed that environmental tobacco smoke caused some lung cancers. But they would not commit themselves to an estimate of the amount. I thought that this was appropriate at the time and it was my view too. Three years ago there were a dozen studies of the subject—most of which showed a greater riks of lung cancer in non-smoking men and women if their spouses smoked than in non-smoking men and women whose spouses didn't smoke. The results varied substantially but this was only to be expected with the numbers of patients. They showed, however, no statistically significant heterogeneity. But it seemed to me that there was a possibility that a woman who was a non-smoker, if married to a smoker, might have smoked a bit more in the past than a non-smoking woman who was married to a non-smoker. I thought that there must be a bias of that sort and, that being so, it was difficult to say that the two lots of non-smokers were at exactly the same risk and could be expected to have the same lung cancer rates apart from their exposure to environmental smoke. Therefore I didn't think that you could put a figure on the size of the risk. Since then Professor Nicholas Wald, who worked with me for many years and is now Professor of Epidemiology at St Bartholomew's, has made some careful analyses of the extent to which non-smokers married to smokers would have to have given incorrect reports of their smoking histories in order to create the quantitative differences that have been observed. He showed conclusively that it is very unlikely that biases of the sort I

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have referred to could account for the results that have been obtained. They might perhaps account for a quarter of the excess, something like that. But this is more than compensated for by the fact that the non-smoker is also exposed to smoke from outside his or her home. When you take that into account as well, the quantitative estimate of the effect of passive smoking that has been made is probably an underestimate rather than an overestimate. So I have now come round to the conclusion that you can put a figure on the number of cases of lung cancer produced by environmental tobacco smoke with some confidence. But it must be less certain than the figure for the effect of active smoking.

BJA: *Besides your research career, did you continue to be involved personally in clinical practice?*
RD: I continued as a clinician with Avery Jones until 1969. All that time Bradford Hill encouraged me to continue to work with Avery Jones because he thought that it was invaluable for an epidemiologist to have some direct knowledge of clinical medicine. I had four beds in Avery's wards all the time until 1969, and treated patients with peptic ulcer and gastric cancer, doing clinical research on their causation and on different forms of treatment. Indeed, I have always thought that one of the more important pieces of research I have ever done was to demonstrate that a bland diet was of no value in the treatment of gastric ulcer. That contributed to saving millions of people from having the miserable diets that used to be imposed on them. But I had beds only for research purposes and held only special research clinics. I never carried responsibility for routine admissions of acute patients.

BJA: *Today if a young man or young woman came to you and said—Professor I've got an interest in mathematics and have qualified in medicine, have written a bit for the College Journal, have got my membership and I am now thinking of a career in research—what would you advise him to do so as truly to acquire the skills of a research worker? Have himself apprenticed to a senior scientists? Go to America for a couple of years? Do a PhD? Take a degree in mathematics? What would you say?*
RD: I don't think it is necessary for a medical person to do a PhD. It is essential in many subjects because it is the certificate of qualification to do research. There are many fields in which you really can't get a research job until you've got a PhD. But medical training is already so long that the acquirement of a PhD is an unreasonable burden. My advice is to get into a good research unit as soon as possible and get on with doing research. I did incidentally want to do a PhD myself. I got my London MD by examination and was sorry that I had never written a thesis. I therefore registered at London University to do a PhD on the aetiology of cancer of the cervix; but before I had completed it Bradford Hill got the university to give me a DSc instead. A PhD really isn't essential for a successful career. My colleague Richard Peto was elected to the Royal Society a few years ago without ever having acquired a PhD because he got into research straight from his MSc and produced such excellent work. My advice to someone going into medical research is that if you can get into a good research group and produce good work, you don't need to worry about degrees. But that I know is not generally true for someone who qualifies in biochemistry or statistics. Peto was quite exceptional.

BJA: *Do you have any worries in your area of science about the continuing strength of the British research base?*
RD: I would rather not express an opinion on what's happened in the last 10 years because, although I have been continuing to do research, I have not been involved in the day to day work of universities; and I am really not *au fait* with the problems facing young people and research departments. I have also been particularly fortunate in being associated with the Imperial Cancer Research Fund. Working for them has been like working for the Medical Research Council, as it used to be in the 1950s. That's to say if you have a good idea you ring them up and they say (or have said until recently), "Get on with it, how much do you want?" So I am really not in a position to comment. There is a lot of first-class research going on, but I know that my senior colleagues are having to devote more and more time to writing out long research applications, something that has restricted the production of American research for the last 20 years. This requirement is spreading in England and I think it is very unfortunate. I still believe that some major sponsors of research should be willing to back individuals and to give them relatively free hands and not to make the financial solvency of research units dependent on preparing long and complicated research applications. It should rather depend on the productivity of their past work.

BJA: *Another question. There was a paper published 40 years ago by yourself and Bradford Hill telling us*

that smoking causes lung cancer. There are still in this country about 100 000 deaths a year related to smoking. But what do you think now about that story, the impact of your paper, the 40 year gap, the continuing mortality? Would you still take the line that the scientist must keep away from over involvement? Or do you feel a need to make that work have its public health bite.

RD: Well, so far as my own position is concerned I am now much more prepared to take an active part. Indeed I have done so in a number of international organizations and in broadcasts. The danger of such activity biasing my future work is by now quite small. So I have changed my views with the passage of time. But that isn't to say that I would advise a young person to become an activist when he first obtains some socially interesting results. I can't say that I have been disappointed by the public's reaction to our work. It never struck me that the reaction would be quick. Smoking was so ingrained in the population. Until the press and the radio and television became convinced of the relationship there really wasn't much hope of getting the message through to the general population. You could get through to scientists and to doctors with your publications, but not to the general public, if every time you had published a report that cigarette smoking caused disease *X*, the media reported that the issue was controversial and that somebody else believed that the disease was caused by something else. That continued to be the position for at least 15 years after 1950. So how could you expect the ordinary person to take the matter seriously? "These scientists", they would say, "They can't agree amongst themselves." So, I never thought the public would take the matter seriously until we had a change of heart by the leading figures in the press and broadcasting. This occurred in the early 1970s and was quickly followed by a big change in the attitude of the public.

BJA: *And conviction at governmental level?*

RD: Until the government was sufficiently convinced of the need to do something effective and particularly to increase taxation, I didn't expect to see any big change. I wrote to Dennis Healey, when he was Chancellor of the Exchequer, on the first occasion that a Chancellor announced in the House that he had increased taxation on tobacco on health grounds, and congratulated him for doing so. I got a personal reply from him, saying that he didn't receive many letters congratulating him on increasing taxation, and he was pleased to get mine. But I have been disappointed by the Government's failure to increase taxation recently and by their failure to ban advertisements. At present young people can reasonably say, "Oh well, smoking can't be all that bad or the Government would never allow tobacco to be advertised in the way it is". So I have been disappointed in those two ways. I have never been disappointed at the failure to persuade children not to take up smoking. My reaction to this was formed early on, in about 1953, when I gave a lecture on smoking and lung cancer at the London School of Hygiene. In the subsequent discussion a man got up at the back of the hall and said that our conclusion was very important and that it obviously meant that we had got to try to get at children to stop them starting to smoke. It was, he said, no good aiming propaganda at adults because they were addicted and you couldn't get them to change. So, he said, we have just got to stop children from taking up the habit. I didn't recognize the man and he turned out to be a representative of the tobacco industry. It was quite clear to me from then on that the industry knew that as long as young adults were smoking, and providing role models for children, it didn't matter how much you tried to educate children not to smoke, because they would not take any notice. I have taken the view ever since then that while education about the harmful effects of smoking should be a part of general biological education in schools, it shouldn't be a specific and separate subject. What you had to do was to get young adults to stop smoking, particularly sportsmen, TV stars and anyone else that children look up to, including doctors, teachers and even parents. I have not been disappointed by children smoking, but I have been by the slowness of the Government's reaction. Much of what has happened in this country in the last 20 years has been encouraging. We have seen a big change in the incidence of lung cancer—and that I find really exciting. Some of the reduction in incidence is due to the introduction of low-tar cigarettes. They are not the whole answer to lung cancer and they don't reduce the risk of most of the other smoking-related diseases, but they do reduce the risk of lung cancer. We now see in this country that the mortality from lung cancer in men under 35 years of age has gone down by 80% from its maximum just after the war and the reduction has gradually spread to older and older people until we now have a situation in which the mortality is coming down in men at all ages under 85. Epidemiological evidence tells us that if you want to predict what is going to happen to cancer mortality in the

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1. DOLL, R
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future you have to examine the trend in young people. We saw the epidemic first appear in young people and it is now fading in them almost as quickly as it came. I am, in consequence, optimistic about the future trend of smoking-related diseases.

BJA: *So the scientific insights in the long run haven't just remained on the shelf?*

RD: They certainly haven't. The worrying thing now of course is the spread of smoking to the developing countries where one can see that the increase in mortality from these smoking-related diseases more than compensates for the decrease in the few countries that have already taken the smoking problem seriously.

BJA: *If you have someone lighting up a cigarette in front of you in a restaurant do you find that is just a cross to be borne, or having spent a lifetime researching these matters does that make you vey uncomfortable? Do you move away, expostulate, send for the head waiter...?*

RD: No, I ignore it. I decided on Bradford Hill's advice not to get involved in public education and to try not to be emotional about the subject. I don't mind in the least if someone in the room lights up a cigarette—it's their decision and their life, not mine. In the last few years, however, as smoking has become less common, I have come greatly to prefer a smoke-free atmosphere. And I am now beginning to get irritated if someone smokes in a restaurant, because I find it actually rather unpleasant.

BJA: *It would be a bold smoker knowingly to light up in front of Richard Doll.*

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